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Dear Dr. Olden:

On behalf of our 750,000 members, People for the Ethical Treatment of Animals (PETA) is appealing to you once again to stop yet another National Toxicology Program (NTP) testing scheme that will cause suffering and death to untold numbers of animals who will be used to re-test already well-characterized chemicals.

On July 22, we wrote to you regarding the NTP's plan to subject more animals to toxicity tests for hexavalent chromium, a well-studied chemical and known human carcinogen. On July 8, we wrote regarding the NIEHS' proposal to retest methanol on animals. Last year, on January 19, May 3, and September 23, we submitted comments on the NTP's proposals to test a number of substances, including natural substances (e.g., grape seed extract), many already well-characterized substances, including metal-working fluids (in a number of cases, data from NTP-conducted studies had been overlooked), and chemicals already covered under the EPA's high production volume (HPV) chemical-testing program.

Although in some cases we submitted lengthy documentation of existing data that the NTP had ignored when it proposed further animal testing and also documented the complete lack of consideration of *in vitro* technologies, all of our comments have gone unanswered and, to the best of our knowledge, no changes were made in the NTP's final recommendations. We therefore turn to you, yet again, to request your intervention in these endless animal testing proposals that emanate from the NTP, that lack all common sense as well as scientific merit.

We are addressing these comments directly to you because your comments at the 2002 Summer Toxicology Forum indicated that you were unaware of — and concerned about — the overlap between the NIEHS' proposal to study methanol with the EPA's ongoing studies. It is these redundant testing proposals that lead to the use by the NTP of an exorbitant number of animals.

Our comments today address the NTP's June 12, 2002, *Federal Register* notice entitled, "Announcement of and Request for Public Comments on Substances Nominated to the NTP for Toxicological Studies and on Study Recommendations Made by the NTP Interagency Committee for Chemical Evaluation and Coordination." Our comments here will reiterate issues we have raised previously in written responses to similar NTP *Federal Register* notices, and then provide an example of wastefulness specific to this particular proposal.

The most glaring omission in the June 12 notice is the complete and total failure to consider the use of *in vitro* technology. The notice states: "The NTP is interested in identifying appropriate new animal models for mechanistic based research, including transgenic or knockout mice, and welcomes comments regarding the use of specific animal models to address scientific questions relevant to the nominated substances and studies under consideration."

As a result, the *Federal Register* notice calls for a large number of animal tests, including tests for the following endpoints: acute, chronic, reproductive and developmental toxicity, carcinogenicity, genotoxicity, hypersensitivity, neurotoxicity, immunotoxocity, and pulmonary toxicity. Animals proposed for use include non-human primates. A number of these endpoints could be studied *in vitro* and, since the NTP is not bound by the restrictions of regulatory agencies, it has absolutely no excuse for failing to consider and encourage the use of *in vitro* assays for these endpoints.

For example, the European Centre for the Validation of Alternative Methods recently validated an *in vitro* (rodent) embryonic stem cell test for the assessment of embryotoxicity. The ability to assess a major landmark in development toxicity *in vitro* can greatly reduce the number of animals killed in the assessment of this endpoint (i.e., by treating embryotoxicants as developmental toxicants without requiring a full developmental toxicity study). Yet this method and strategy have been completely overlooked by the NTP, as have other *in vitro* methods.

From a scientific standpoint, it is ridiculous that the NTP continues to ignore the recommendations of its own scientists by repeatedly calling for more animal carcinogenicity data. As we have pointed out repeatedly in previous comments, the lack of relevance and reliability of rodent bioassays for this endpoint has been extensively documented (see, for example, our comments to you dated July 22). Yet the NTP insists on requesting an endless number of these useless tests.

As a further note, there is absolutely no reason for the NTP to be requesting further testing at this point on substances that are part of the EPA's high production volume (HPV) chemical testing program. This represents the height of redundancy and wastefulness, and simply illustrates further the NTP's complete lack of concern with the number and suffering of animals it is condemning to death.

For the purposes of these comments, we would like to focus on just one of the chemicals the NTP is suggesting requires further animal studies. The *Federal Register* notice lists the substance turpentine as nominated by United Auto Workers' International Union for further chronic toxicity and carcinogenicity studies, with the rationale given that there is "insufficient chronic toxicity information" for this chemical. The NTP's Interagency Committee for Chemical Evaluation and Coordination concurs.

Turpentine oil is a flammable, toxic liquid that has long been known to cause serious adverse health effects in many species, including humans. Turpentine is a dermal, ocular, and respiratory irritant. Turpentine causes central nervous system depression and harmful gastrointestinal, urinary tract, and respiratory effects. It has also been implicated as a reproductive toxicant. Exposure to turpentine may cause nausea, vomiting, diarrhea, headache, dizziness, bladder irritation, chest pain, visual disturbances, choking, dyspnea, pulmonary edema, convulsions, fever, tachycardia, and death due to respiratory failure. The Occupational Safety and Health Administration, the National Institute for Occupational Safety and Health, and the American Conference of Governmental Industrial

Hygienists all concur that an acceptable time-weighted average exposure limit over a full workday is 100 ppm (560 mg/m^3).

Chronic effects in humans have been observed in employees who routinely come into contact with turpentine. Chronic skin exposure to turpentine may produce a hypersensitivity reaction, with dermatitis and/or eczema (1). A case-control study of workers in particleboard, plywood, sawmill, and formaldehyde glue factories showed a statistically significant association between chronic exposure (longer than 5 years) to terpenes (the principal component of turpentine) and the development of respiratory tract cancers (2). Occupational studies of workers with chronic exposures to turpentine have demonstrated associations between turpentine and adverse reproductive and developmental effects (3,4).

Many acute, chronic, and mechanistic animal studies have been conducted with turpentine. Turpentine has been identified as an eye, mucous membrane, and skin irritant and a central nervous system depressant in animals. Dermal application of turpentine has produced tumors in some species of animals in some experiments. Arterial, cardiac, and skeletal muscle lesions caused by turpentine-induced renal alterations were observed in rabbits (5). Adverse neurological effects have been observed in chronic animal studies (6). Liver damage has also been observed in animal studies (7,8).

Clearly, turpentine is associated with many chronic and acute hazards. Additional animal data are not needed to attempt to model how poisonous this chemical is to humans. Efforts need to be directed toward improved medical surveillance in the workplace as well as towards administrative and engineering controls of turpentine exposure. Steps should be taken to prevent worker exposure to this chemical and to reduce exposure well below permissible levels. For example, turpentine can often be replaced in the occupational setting by the petroleum product white spirit. Research efforts would be best directed toward occupational epidemiological studies of workers who are frequently exposed to turpentine such as woodworkers and painters, increased medical monitoring, and clinical observations of accidental or intentional turpentine poisoning.

Dr. Olden, surely you will agree that no more animals need to die to re-test turpentine, welding fumes, and abrasive blasting agents. We once again urge you to intervene in this important matter.

Sincerely,

/S/

Jessica Sandler, MHS
Federal Agency Liaison

cc: Dr. Scott Masten

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